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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,233	09/25/2006	Stephen Robert Wedge	056291-5303	3400

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EXAMINER	
NATHAN, SHYAM	

ART UNIT	PAPER NUMBER
1611	

MAIL DATE	DELIVERY MODE
10/29/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,233	WEDGE, STEPHEN ROBERT	
	Examiner	Art Unit	
	SHYAM NATHAN	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-18,20,21 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-18,20-21,24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/14/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 9,11-12 and 22-23 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/14/2008. Applicant did not provide reason for traversal so, the requirement is still deemed proper and is therefore made FINAL.

A new claim 24 has been added. Claims 15-18,20-21, and 24 are pending in this application. This is the first Office action on the merits of the claims.

Priority

Applicant's claim for the benefit of a prior-filed international application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. The earliest effective US filing date afforded the instantly claimed invention is 03/22/2005, the filing date of PCT/GB05/01079.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 15-21 and 24 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of copending Application No. 10/563439; 10563,440; 10/594,233; 10/594,234; 11,663,912 in view of Lee (US Pub No. 2002/0002162; Pub.Date Jan.3,2002.)

The limitation of the claims in the instant application is drawn to AZD2171 combined with 5-FU and CPT-11. The limitation of the claims of application 10/563439 is drawn to AZD2171 and ZD1839, which is an anti-tumor agent. But the instant application does not disclose 5-FU and CPT-11.

Lee '162 , teaches therapies for treatment of cancer , that further, teach a synergistic method for the treatment of cancer in a mammalian specie[0002,0011] which comprises a vascular endothelial growth factor receptor tyrosine kinase inhibitor, ZD6474 [0082],(Also an anti-tumor agent) in conjunction with CPT-11 [0074, Table 1], 5-FU or %-fluorouracil[0072,Table 1] for the treatment of breast, pancreas, bladder colon lung, skin, **colorectal**, non-small cell lung cancer and mesothelioma.[0059-0067]. Lee also teaches of radiation therapy that includes but is not limited to x-rays or gamma rays [0068], that is usually given at the same time as the cancer treating method

discussed above. The 5-Fluorouracil and CPT-11 used in the method of Lee '162 can also be added to the VEGF tyrosine kinase inhibitor (AZD2171) of copending Application No. 10/563439.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have added 5-FU and CPT-11 to avascular endothelial growth factor receptor tyrosine kinase inhibitor (In the case of Lee '162, ZD6474, which could be substituted for ZD1839 or AZD2171) to provide further cytoxic agents for a method for the treatment of cancer.

Copending applications: 10563,440; 10/594,235; 10/594,234; 11,663,912 are also provisionally rejected on the ground of nonstatutory obviousness-type double patenting because their claims can be modified by Lee for the same reasons stated above.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee (US Pub No. 2002/0002162;Pub.Date Jan.3,2002 in view of Hilberg et al.(WO/2004/096224;Prior.date 02/29/2003) .

Instant claims 15-17 are drawn to a method for the treatment of a cancer involving a solid tumor in a warm-blooded animal in need thereof, which comprises administering to said animal an effective amount of AZD2171(in form of a free base) or a pharmaceutically acceptable salt thereof excluding an AZD2171 maleate salt, before ,after or simultaneously with an effective amount of 5-FU, CPT-11 and ionizing radiation.

Lee '162 , teaches therapies for treatment of cancer , that further, teach a synergistic method for the treatment of cancer in a mammalian specie[0002,0011] which comprises a vascular endothelial growth factor receptor tyrosine kinase inhibitor, ZD6474 [0082], in conjunction with 5-Fluorouracil [0072,Table 1] and CPT-11 [0074,Table 1] for the treatment of breast, pancreas, bladder colon lung, skin colorectal,

non-small cell lung cancer and mesothelioma.[0059-0067]. Lee also teaches of radiation therapy that includes but is not limited to x-rays or gamma rays [0068], that is usually given at the same time as the cancer treating method discussed above.

But, Lee '162 does not teach of AZD2171 as a vascular endothelial growth factor receptor tyrosine kinase inhibitor.

Hilberg et al.(WO/2004/096224;Prior.date 02/29/2003) teaches of AZD2171 as an vascular endothelial growth factor receptor tyrosine kinase inhibitor(pg.34 lines 1-7)

It would be prima facie obvious to one skilled in the art to substitute the AZD2171 in Hilberg et al. for the ZD6474 taught in Lee '162 because ZD6474 can be substituted for AZD2171 because they are both vascular endothelial growth factor receptor tyrosine kinase inhibitors, which would give them the same mode of action. ZD6474 is taught by itself without a salt being mentioned, therefore, it is a free base. Furthermore, it would be obvious that radiation involving x-rays and gamma rays can be ionising radiation.

Claim 18, 20-21,24 are rejected under 35 U.S.C. 103(a) as being unpatentable over : Lee (US Pub No. 2002/0002162;Pub.Date Jan.3,2002 in view of Hilberg et al.(WO/2004/096224;Prior.date 02/29/2003) as applied to claim 21-24,27-28 above, and further in view of Lane et al (US Pub No. 2004/0147541; PCT filed 02/18/2002).

Instant claims 18, 20-21, 24 are drawn to a method for the treatment of a cancer involving a solid tumor in a warm-blooded animal in need thereof, which comprises administering to said animal an effective amount of AZD2171 salt before, after or

simultaneously with an effective amount of 5-FU, CPT-11 and ionizing radiation for the treatment of colorectal cancer, which is a solid tumor cancer.

Lee (U.S. Pub. No: 2002/0002162; Pub. Date Jan.3, 2002) teaches of a vascular endothelial growth factor receptor tyrosine kinase inhibitor, ZD6474, in conjunction with 5-Fluorouracil [0072,Table 1] and CPT-11 [0074,Table 1], for the treatment of breast, skin, colon, and **colorectal cancer** [0059-0067]. And Hilberg et al.(WO/2004/096224;Prior.date 02/29/2003) teaches of AZD2171 as an vascular endothelial growth factor receptor tyrosine kinase inhibitor(pg.34 lines 1-7) ZD6474 can be substituted for AZD2171 because they are both vascular endothelial growth factor receptor tyrosine kinase inhibitors, which would give them the same mode of action. But, the Lee references do not teach the maleate salt of AZD2171.

Lane et al teaches of a method for treating solid tumors [0013], that comprise VEGF receptor tyrosine kinase inhibitors, such ZD6474[0060] (which can be substituted for AZD2171), and salts thereof [0073] -(which states that any subject matter relating to compounds in Lane et al., such as pharmaceutically acceptable salts can be incorporated in the Lane et al reference). . Furthermore, Lane et al. in paragraph 0073 discloses that any subject matter relating to the compounds is here incorporated into the application Lane et al. by reference. This includes pharmaceutically acceptable

salts, which would include maleate salts of ZD6474. (which can be substituted for the maleate salts of AZD2171).

It would be prima facie obvious to one skilled in the art to to combine the above references because both Lee and Lane et al. are drawn towards methods for the treatment of cancer and tumors that involve VEGF receptor tyrosine kinase inhibitors , such as AZD2171. Furthermore, it would be obvious to one skilled in the art to substitute the salt of a vascular endothelial growth factor receptor tyrosine kinase inhibitors, such as ZD6474, for AZD2171, because they are both vascular endothelial growth factor receptor tyrosine kinase inhibitors, which would give them the same mode of action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHYAM NATHAN whose telephone number is (571)270-5753. The examiner can normally be reached on Mon-Thurs 8:30a.m. - 5:00p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SN

/Sharmila Gollamudi Landau/

Supervisory Patent Examiner, Art Unit 1611